PATENT
Atty. Docket No.: 401-UTL-0 (18528.010)

REMARKS

Claims 1, 8 and 33-63 are currently pending. Claims 2-7 and 9-32 were previously canceled without prejudice or disclaimer. New claims 64-70 have been added, and support for these claims can be found throughout the specification, and at least on page 4, lines 22-27, on page 6, lines 23-25, on page 7, lines 10-12 and in Table 1. No new matter has been introduced. Upon entry of the present amendment, claims 1, 8, and 33-70 will be pending.

Information Disclosure Statement

Applicants note with appreciation that the Information Disclosure Statement filed 11 October 2005 has been received and considered by the Examiner.

Withdrawn Objections and/or Rejections

Applicants note with appreciation that the rejection of claims 1, 33, 38, 42, 48-50 and 52-54 under 35 U.S.C. 102(b) as being anticipated by Morley has been withdrawn.

Applicants note with appreciation that the rejection of claim 51 under 35 U.S.C. 103(a) as being unpatentable over Morley in view of Naslund has been withdrawn.

Rejections Under 35 U.S.C. § 112, First Paragraph – Enablement

Claims 1, 8, 33-46 and 48-63 were rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement for use of the claimed invention commensurate in scope with the claims. Applicants respectfully disagree with this rejection to the extent it is maintained in light of the amended claims.

As exemplified at least by US Patents 5,574,010, 5,604,203, 5,696,093, and 6,046,167, PYY agonists were known as such at the time of filing. These Patents describe the PYY agonist molecules themselves and the fact that they have agonist activity. The Examiner alleges that the agonists in the cited references were not described "in the context of reducing nutrient availability, food intake or body weight" (Office Action, 23 November 2005, page 5). However, the instant specification teaches how to use the claimed PYY and PYY agonists. The Examiner appears to be contesting that the PYY

agonists claimed can be used in the methods of the invention. The Examiner states that "[a]n antagonist may bind the PYY receptor; but it does not make the antagonist an agonist" (Office Action, 23 November 2005, page 5). Applicants respectfully submit that a person of ordinary skill in the art would understand the difference between an agonist and an antagonist. It is well known that an agonist is a compound that binds a PYY receptor and stimulates receptor activation, whereas an antagonist may bind a receptor, but it does not stimulate receptor activation. Applicants note that, in the specification as filed, a PYY agonist is defined as having at least these characteristics; specifically, a PYY agonist is "any compound which elicits an effect of PYY to reduce nutrient availability, for example a compound (1) having activity in the food intake, gastric emptying, pancreatic secretion, or weight loss assays described herein in Examples 1, 2, 5, or 6, and (2) which binds specifically in a Y receptor assay (Example 10) or in a competitive binding assay with labeled PYY or PYY[3-36] from certain tissues having an abundance of Y receptors, including e.g., area, postrema (Example 9), wherein the PYY agonist is not pancreatic polypeptide." (See page 5, lines 24-25 of the specification; emphasis added). Applicants have claimed PYY agonists which meet a first criterion of Y-receptor binding and meet a second criterion of receptor activation, in that these PYY agonists initiate a specific set of pharmacological responses (e.g., reducing caloric efficiency, nutrient availability, body weight, body weight gain, or food intake). PYY antagonists are not included in the claimed genus. Therefore, the specification provides ample exemplification of PYY agonists, as well as specific teachings for assessing the ability of any member of the genus of PYY agonists to activate a receptor-mediated pharmacological response (e.g., reduction of food intake, body weight or body weight gain, caloric efficiency and nutrient availability), allowing one of ordinary skill in the art to make and use the claimed invention. Thus, Applicants have provided an enabling statement, and, under established law, this statement must be taken as enabling unless the Examiner can provide evidence to the contrary.

Limitation of coverage to species which have been proven to work or to "preferred" materials, leaves potential avenues for easily circumventing the claims by copiers, and conflicts with the basic purpose of the patent system. *In re Goffe*, 542 F.2d 564, 567 (CCPA 1976). Moreover, it is incumbent upon the Patent Office, whenever a

rejection on the basis of enablement is made, to explain why it doubts the truth or accuracy of any statement made in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 439 F.2d 220, (CCPA 1971). The Examiner has provided no evidence or reasoning which explains why the Patent Office doubts the truth or accuracy of Applicants' enablement of the invention as defined in the pending claims. Because the Examiner has failed to produce any such evidence, he appears to be relying on personal knowledge. "When a rejection in an application is based on facts within the personal knowledge of an employee of the Office, the data shall be as specific as possible, and the reference must be supported, when called for by the applicant, by the affidavit of such employee, and such affidavit shall be subject to contradiction or explanation by the affidavits of the applicant and other persons." (See 37 CFR 1.104(d)(2)). Applicants respectfully request such a reference or an affidavit.

Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 8, 33-46 and 48-63 for lack of enablement.

Rejections Under 35 U.S.C. § 112, First Paragraph – Written Description

Claims 1, 8, 33-46 and 48-63 were rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking written description. The Examiner alleges that "[t]he specification merely discloses two compounds, a human PYY of SEQ ID NO: 2 and PYY(3-36) of SEQ ID NO: 3, which are not sufficiently representative of the claimed genus of PYY agonists. There is no defined relation between function and structure of the PYY agonists. There is even no identification of any particular portion of the structure that must be conserved," and "in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genus of PYY agonists and the genus of agonists of a GLP-1, an exendin, and an amylin." (Office Action, 23 November 2005, pages 7-8). Applicants respectfully disagree with this rejection to the extent it is maintained in light of the amended claims.

As stated above, the specification as filed sets forth ample description of PYY agonists with the requisite ability to activate a receptor-mediated response. For example, agonists are described in US Patent 5,604,203, which is incorporated by reference in

Applicants' specification, as filed. According to the M.P.E.P., information contained in another document may be incorporated by reference to the document in the text of the specification. "The information incorporated is as much a part of the application as filed as if the text was repeated in the application, and should be treated as part of the text of the application as filed." (M.P.E.P. 2163.07(b)). Furthermore, assays are provided for determining whether a PYY agonist or PYY agonist analog has pharmacological effects. Description is also provided at least on page 7, lines 23-30 of the specification for the administration of a PYY or PYY agonist with a GLP-1, an exendin, an amylin, their agonists, or any combination thereof, as provided in claim 51, and, furthermore, these molecules are known in the art.

Nonetheless, without acquiescence to the rejection and solely to advance prosecution, Applicants have amended claims 1, 8, 34-41, 43-46, 52, 53 and 55-58 (and claims 33, 48, 54, 59-61 and 63 depend from the amended claims) to recite the additional identifying functional characteristics of said PYY agonists: "wherein the PYY agonist has pharmacological effects at a Y2, Y5 or Y7 receptor greater than those at a Y1 receptor." Thus, Applicants have provided sufficient description of the genus, including disclosure of structures of PYY and PYY agonists, as well as additional distinguishing identifying characteristics of the genus and the rejection is believed to be overcome. Applicants submit that the skilled artisan would readily recognize that the Applicants were in possession of the claimed invention. Applicants, therefore, respectfully request reconsideration and withdrawal of the rejection of claims 1, 8, 33-46 and 48-63 under 35 U.S.C. § 112, first paragraph.

Rejections Under 35 U.S.C. § 112, Second Paragraph – Indefiniteness

Claims 1, 8, 34-41 and 52-54 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, with respect to the phrases "desirous of" and "in need thereof," the Examiner alleges that "[i]t is unclear how such a limitation, which represents a mental process, limits the subject recited in the claims" (Office Action, 23 November 2005, page 10). The Examiner further states that "[i]t is unclear how a person of skill in the art could determine whether a

mouse wishes or desires to be treated with PYY or a PYY agonist" (Office Action, 23 November 2005, page 11) and that the mongrel dog of Yoshinaga "was in need of treatment; otherwise such a treatment would not have been performed" (Office Action, 23 November 2005, page 14). Applicants respectfully disagree with this rejection to the extent it is maintained in light of the amended claims. The courts have held that the phrase "in need thereof" is meaningful, and that "the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose." (*Jansen v. Rexall Sundown, Inc.*, 342 F.3d at 1333).

Nonetheless, without acquiescence to the rejection and solely to advance prosecution, Applicants have amended claims 1, 8, 34-41, 52, 53 and 55 to more particularly point out and distinctly claim that it is the subject "who desires to reduce" food intake, body weight, body weight gain or appetite, and not the person administering the treatment. Applicants respectfully submit that a person of ordinary skill in the art would easily be able to identify the claimed subject population, i.e., a subject who desires, or is in need of the claimed method, and those subjects which cannot be determined to desire or be in need of treatment are not claimed. Applicants respectfully request withdrawal of the rejection.

Claims 8, 33-36, 43-51, 54 and 56-63 were also rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite because they recite "a peripheral parenteral route," and the Examiner alleges that neither the specification nor the art define the phrase unambiguously. "Peripheral parenteral" was also objected to as a minor informality. The Examiner states "[t]wo adjectives cannot be used consecutively." Applicants disagree. The phrase "peripheral parenteral" is not indefinite or grammatically incorrect. Examples of the occurrence of two consecutive adjectives in a sentence are ubiquitous in the English language. Furthermore, section 608.01(g) of the M.P.E.P states that "[a]n applicant is ordinarily permitted to use his or her own terminology, as long as it can be understood. Necessary grammatical corrections, however, should be required by the examiner, but it must be remembered that an examination is not made for the purpose of securing grammatical perfection." The proper test for indefiniteness is whether every claim term, read in view of the specification, would allow a person of ordinary skill in the art to understand what is claimed. Throughout the specification, peripheral administration

of PYY is described and is compared and contrasted with central administration of PYY into the central nervous system (for example, into the hypothalamus or hindbrain/brainstem, as described on page 2, lines 3-5 and lines 18-23). Parenteral administration is understood in the art and is set forth, at least, at page 14, lines 6-8. Nonetheless, without acquiescence to the rejection and solely to advance prosecution, Applicants have amended claims 8, 33-36, 43-51, 54 and 56-63 so that the adjectives do not appear consecutively. Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

Rejections Under 35 U.S.C. § 102(b)

Claims 1, 8, 33-42, 47-49 and 52-60 and 62 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Yoshinaga, et al., (*Am. J. Physiol.* 263:G695-701, 1992). The Examiner alleges that "(s)ince Yoshinaga et al. teach a method of administering to a subject the same agent (PYY or PYY agonist) in the same dose range by the same route of administration as that of the instantly claimed method, the intended uses and properties of the PYY or PYY agonist recited in the claims are inherent to the method taught by Yoshinaga, et al." (Office Action 23 November 2005, page 12). Applicants respectfully traverse the rejection to the extent it is maintained in light of the amended claims, because Yoshinaga does not teach, expressly or inherently, each element recited in the claims.

Yoshinaga teaches that administration of PYY and PYY(3-36) to dogs inhibits pancreatic exocrine and gastric acid secretion. Yoshinaga does not teach or suggest reducing caloric efficiency of claims 1 and 38, nor reducing food intake of claims 8, 34, 39 and 56, nor reducing appetite of claims 35, 36, 40 and 57, nor reducing nutrient availability of claims 37, 41 and 58, nor reducing weight, weight gain or increasing weight loss of claims 52, 53, or 55. Furthermore, as amended, claims 1, 8, 34-41, 52, 53 and 55 require administration to a subject who desires to reduce caloric efficiency, nutrient availability, food intake, appetite, body weight or body weight gain, or to increase weight loss. As amended claims 56-58 (as well as claims dependent thereon) require that the subject be in need of reduction of food intake, appetite or nutrient availability. Again, the phrase "in need thereof" has been held to be meaningful in the

courts. (*Jansen v. Rexall Sundown, Inc.*, 342 F.3d at 1333). Thus, Yoshinaga cannot render unpatentable by inherency the subject population of the claimed invention.

Because the disclosure of Yoshinaga does not teach, expressly or inherently, each element recited in the claims, the 102(b) rejection is improper. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 8, 33-42, 47-49 and 52-60 and 62 under 35 U.S.C. § 102(b).

Claims 1, 8, 33-42, 47-50 and 52-62 were rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Okada, et al., (The Endocrine Society 75th Annual Meeting Program & Abstract, page 180, Abstract 520B, 1993). Applicants respectfully traverse the rejection, because Okada does not teach, expressly or inherently, each element recited in the claims.

Okada teaches that administration of PYY to rats fed a diet containing high-fat diet (deriving 56% of its calorie content from fat) reduces food intake, and that PYY may be a satiety factor for a high-fat meal. The Examiner states that Applicants' claim of a method of reducing non-high fat food intake or appetite "still encompasses 'medium fat food' or 'fat food'" and that "[s]ince Okada et al., teach that PYY is a satiety factor for a fat meal, the reference of Okada et al. meets the limitations of claims 8 and 35" (Office Action 23 November 2005, page 16). The Examiner appears to be arguing that the high-fat meal of Okada encompasses a meal containing any fat at all. Applicants disagree. Okada does not teach or suggest that administration of PYY has any effect on food intake of any food other than a diet containing 56% fat. Therefore, at most, Okada teaches that PYY may influence the state of satiation of a rat upon being fed a high-fat diet.

Okada does not teach PYY[3-36] of claim 47. Okada does not teach the receptor affinities of claims 38-42 and 62. Okada does not teach or suggest reducing caloric efficiency of claims 1 and 38, nor reducing appetite of claims 35, 36, 40 and 57, nor reducing nutrient availability of claims 37, 41 and 58, nor reducing weight, weight gain or increasing weight loss of claims 52, 53, or 55 in the claimed subject population. Furthermore, as amended, claims 1, 8, 34-41, 52, 53 and 55 require administration to a subject who desires to reduce caloric efficiency, nutrient availability, food intake, appetite, body weight or body weight gain, or to increase weight loss. As amended claims

56-58 (as well as claims dependent thereon) require that the subject be in need of reduction of food intake, appetite or nutrient availability. As amended claims 56-58 (as well as claims dependent thereon) require that the subject be in need of reduction of food intake, appetite or nutrient availability. Thus, Okada cannot render unpatentable by inherency the claimed subject population.

Because the examiner has not established that each element required by the claims is expressly or inherently anticipated by Okada, Applicants respectfully submit that the 102(b) rejection is improper. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 8, 33-42, 47-50 and 52-62 under 35 U.S.C. § 102(b).

Rejections Under 35 U.S.C. § 103(a)

Claims 44, 46 and 63 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Okada. The Examiner alleges that the lowest dosage administered to Okada's rats reads on the dose range of PYY claimed in the instant invention, and that "it would have been obvious to one having ordinary skill in the art at the time the invention was made to administer PYY to a human subject to reduce appetite or food intake with a reasonable expectation of success in view of the teachings of Okada et al. on the rats." (Office Action 23 November 2005, page 17). Applicants disagree and respectfully request reconsideration and withdrawal of these rejections.

The teachings of Okada fail to satisfy the criteria necessary for rendering the claimed invention obvious. Firstly, the reference or teachings must teach or suggest each and every limitation of the claimed invention. Okada teaches that administration of PYY to (normal) Sprague-Dawley rats is associated with a reduction of high-fat food intake. Okada does not teach or suggest the administration of PYY to subjects who desire or are in need of reducing food intake or appetite, or who have a disorder which can be treated by reducing caloric efficiency, nutrient availability, body weight, weight gain, food intake or appetite, or increasing weight loss. In fact, Okada is completely silent with regard to the effects of PYY administration on reduction of caloric efficiency, nutrient availability, appetite, body weight, weight gain, or increasing weight loss. Furthermore, it is evident from the art known at the time of filing the instant invention that the claimed

invention is not obvious. For example, Morley et al., expressly teaches that the effects of PYY on food intake and body weight are separable and not necessarily related. "[P]eripherally, PYY caused weight loss, without altering food intake." (Morley, et al., (1987) *Life Sci.* 41:2157-2165).

Secondly, a determination of obviousness is not based on what a person skilled in the art might try or find obvious to try. The standard for rendering a claimed invention obvious is that the prior art must suggest to those of ordinary skill in the art that they should have made the claimed invention and that they would have had a reasonable expectation of success. (*In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 837 F.2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988)). One of skill in the art would readily appreciate that there are physiological and metabolic differences between normal rats and humans who desire or are in need of reducing caloric efficiency, nutrient availability, food intake, appetite, body weight, body weight gain, or of increasing weight loss. There is no basis to assert or assume, *a priori*, that a treatment having a particular affect on normal rats fed a high-fat diet would have the same impact on the claimed subject population. Prior to Applicants' disclosure, one of skill in the art would not have had a reasonable expectation of success in applying the teachings of Okada to the treatment of subjects desiring or in need of treatment to reduce caloric efficiency, nutrient availability, weight, weight gain, food intake or appetite, or to increase weight loss, as required by the pending claims.

At most, in light of Okada, administration of PYY to subjects desiring or in need of treatment to reduce caloric efficiency, nutrient availability, weight, weight gain, food intake or appetite, or to increase weight loss may have been obvious to try. However, the MPEP and the courts have clearly articulated that obvious to try is not the standard for rendering a claimed invention obvious. MPEP 2143.02; *In re Rinehart*, 531 F.2d 1048 (CCPA 1976); *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-08 (Fed. Cir. 1991). The Examiner has failed to make a *prima facie* case that Okada renders the claimed invention obvious because not all the elements of the claimed invention are found within the teachings of Okada, the reference provides no motivation to modify those teachings, and one of ordinary skill in the art would not have a reasonable

expectation of success. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Claim 51 was rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Okada in view of Naslund, et al. (*Int. J. Obes. Relat. Metab. Disord.* 23:304-311, 1999). The Examiner alleges that "It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method taught by Okada et al. to administer GLP-1 in combination with PYY with a reasonable expectation of success. One would have been motivated to do so because GLP-1 has been clearly shown to decrease feelings of hunger and reduces energy intake as taught by Naslund et al. and the combination of GLP-1 with PYY would be expected to be successful, since they are both taught to have the same effect." (Office Action 23 November 2005, page 18). Applicants respectfully request withdrawal of this rejection, for the reasons given above with respect to the Okada reference, and also because the Examiner has failed to establish a *prima facie* case of obviousness.

Neither Okada nor Naslund teaches the co-administration of a PYY or a PYY agonist with any other compound. The fact that references can be combined is not sufficient to establish an obviousness rejection; the references must contain the explicit teaching or suggestion motivating the combination. Furthermore, Naslund merely measures endogenous plasma levels of PYY, and does not teach or suggest **administration** of **exogenous** PYY, PYY agonists, exendin, amylin, their agonists, or any combination thereof. The courts have ruled that that the mere possibility that the prior art can be modified does not itself provide the requisite motivation to do so. (See *In re Dien*, 152 U.S.P.Q. 550 (C.C.P.A. 1967)). Again, neither Naslund nor Okada teaches or suggests the combination, and the Examiner's conclusory statement that the combination would be obvious is not evidence of sufficient motivation to impel the skilled artisan to do what Applicants have done. The Federal Circuit court has ruled that "(b)road conclusory statements regarding the teaching of multiple references standing alone are not 'evidence.'" *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999).

Okada does not teach or suggest methods of reducing caloric efficiency, appetite body weight or body weight gain, or nutrient availability. Neither does Okada teach the

claimed subject population, nor the administration of PYY in combination with "a GLP-1, an exendin, an amylin, their agonists, or any combination thereof." The deficiencies of Okada are not cured by the addition of Naslund. Moreover, the Examiner has pointed to nothing in the cited references or in the art to suggest their combination, and even if combined, the references do not teach all the elements of the claimed invention. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 51 under 35 U.S.C. § 103(a).

Conclusion

In light of the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of all objections and rejections set forth in the Office Action of 23 November 2005. Further, Applicants believe all claims presently under consideration to be in a condition for allowance and request issuance of a Notice of Allowance at the Examiner's earliest convenience.

Should the Examiner have any remaining questions regarding the subject invention or its patentability, Applicants encourage the Examiner to contact the undersigned to discuss any issues remaining.

Respectfully submitted,

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